SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amoxicillin 250 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains amoxicillin trihydrate equivalent to 250mg amoxicillin.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard.
Size 2 for the 250mg capsules, with a scarlet/ivory opaque hard gelatin capsule with 'AMOX 250' printed on the capsule shell.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Amoxicillin Capsules are indicated for the treatment of the following adults and children (see sections 4.2, 4.4 and 5.1):

- Acute bacterial sinusitis
- Acute otitis media
- Acute streptococcal tonsillitis and pharyngitis
- Acute exacerbations of chronic bronchitis
- Community acquired pneumonia
- Acute cystitis
- Asymptomatic bacteriuria in pregnancy
- Acute pyelonephritis
- Typhoid and paratyphoid fever
- Dental abscess with spreading cellulitis
- Prosthetic joint infections
- *Helicobacter pylori* eradication
- Lyme disease

Amoxicillin Capsules are also indicated for the prophylaxis of endocarditis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

The dose of Amoxicillin Capsules that is selected to treat an individual infection should take into account:

- The expected pathogens and their likely susceptibility to antibacterial agents (see section 4.4)
- The severity and the site of the infection
- The age weight and renal function of the patient: as shown below

The duration of therapy should be determined by the type of infection and the response of the patient, and should generally be as short as possible. Some infections require longer periods of treatment (see section 4.4 regarding prolonged therapy).

Adults and children ≥40 kg

Indication*	**Dose***
Acute bacterial sinusitis	250mg to 500mg every 8 hours or 750mg to 1g every 12 hours For severe infections 750mg to 1g every 8 hours Acute cystitis may be treated with 3g twice daily for one day
Asymptomatic bacteriuria in pregnancy	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute cystitis	
Acute otitis media	500mg every 8 hours, 750mg to 1g every 12 hours For severe infections 750mg to 1g every 8 hours for 10 days
Acute streptococcal tonsillitis and pharyngitis	
Acute exacerbations of chronic bronchitis	
Community acquired pneumonia	500mg to 1g every 8 hours
Typhoid and paratyphoid fever	500mg to 2g every 8 hours
Prosthetic joint infections	500mg to 1g every 8 hours
Prophylaxis of endocarditis	2g orally, single dose 30 to 60 minutes before procedure
Helicobacter pylori eradication	750mg to 1g twice daily in combination with a proton pump inhibitor (e.g. omeprazole, lansoprazole) and another antibiotic (e.g. clarithromycin, metronidazole) for 7 days

Lyme disease (see section 4.4)	Early stage: 500mg to 1g every 8 hours up to a maximum of 4g/day in divided doses for 14 days (10 to 21 days) Late stage (systemic involvement): 500mg to 2g every 8 hours up to a maximum of 6 g/day in divided doses for 10 to 30 days
* Consideration should be given to the official treatment guidelines for each indication	

Children <40 kg

Children may be treated with Amoxicillin capsules, dispersible tablets suspensions or sachets.

Amoxicillin Paediatric Suspension is recommended for children under six months of age.

Children weighing 40 kg or more should be prescribed the adult dosage.

Recommended doses:

Indication[+]	**Dose**[+]
Acute bacterial sinusitis	20 to 90mg/kg/day in divided doses*
Acute otitis media	
Community acquired pneumonia	
Acute cystitis	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute streptococcal tonsillitis and pharyngitis	40 to 90mg/kg/day in divided doses*
Typhoid and paratyphoid fever	100mg/kg/day in three divided doses
Prophylaxis of endocarditis	50mg/kg orally, single dose 30 to 60 minutes before procedure
Lyme disease (see section 4.4)	Early stage: 25 to 50mg/kg/day in three divided doses for 10 to 21 days Late stage (systemic involvement): 100mg/kg/day in three divided doses for 10 to 30 days
+ Consideration should be given to the official treatment guidelines for each indication. *Twice daily dosing regimens should only be considered when the dose is in the upper range.	

Elderly

No dose adjustment is considered necessary.

Renal impairment

GFR (ml/min)	**Adults and children**	**Children <40kg** [#]

	≥40kg	
greater than 30	no adjustment necessary	no adjustment necessary
10 to 30	maximum 500mg twice daily	15mg/kg given twice daily (maximum 500mg twice daily)
less than 10	maximum 500mg/day	15mg/kg given as a single daily dose (maximum 500mg)
[#] In the majority of cases, parenteral therapy is preferred.		

In patients receiving haemodialysis
Amoxicillin may be removed from the circulation by haemodialysis.

	Haemodialysis
Adults and children ≥40kg	15mg/kg/day given as a single daily dose. Prior to haemodialysis one additional dose of 15mg/kg should be administered. In order to restore circulating drug levels, another dose of 15mg/kg should be administered after haemodialysis.

In patients receiving peritoneal dialysis
Amoxicillin maximum 500mg/day.

Hepatic impairment
Dose with caution and monitor hepatic function at regular intervals (see sections 4.4 and 4.8)

Method of administration
Amoxicillin Capsules are for oral use.

Absorption of Amoxicillin Capsules is unimpaired by food.

Therapy can be started parenterally according to the dosing recommendations of the intravenous formulation and continued with an oral preparation.

Swallow with water without opening capsule.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients listed in section 6.1. History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).

4.4 Special warnings and precautions for use

Hypersensitivity reactions
Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents (see section 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy (see section 4.3). These reactions are more likely to occur in persons with a history of penicillin hypersensitivity to beta-lactam antibiotics and in atopic individuals. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8). Presenting of such reactions can include chest pain occurring in association with an allergic reaction to amoxicillin therapy (see section 4,8). If an allergic reaction occurs, amoxicillin therapy must be discontinued and appropriate alternative therapy instituted.

Drug-induced enterocolitis syndrome (DIES) has been reported mainly in children receiving amoxicillin (see section 4.8). DIES is an allergic reaction with the leading symptom of protracted vomiting (1-4 hours after drug intake) in the absence of allergic skin or respiratory symptoms. Further symptoms could comprise abdominal pain, diarrhoea, hypotension or leucocytosis with neutrophilia. There have been severe cases including progression to shock.

Non-susceptible microorganisms

Amoxicillin is not suitable for the treatment of some types of infection unless the pathogen is already documented and known to be susceptible or there is a very high likelihood that the pathogen would be suitable for treatment with amoxicillin (see section 5.1). This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.

Convulsions

Convulsions may occur in patients with impaired renal function or in those receiving high doses or in patients with predisposing factors (e.g. a history of seizures, treated epilepsy or meningeal disorders (see section 4.8).

Renal impairment

In patients with renal impairment, the dose should be adjusted according to the degree of renal impairment (see section 4.2).

Skin reactions

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP, see section 4.8). This reaction requires amoxicillin discontinuation and contra-indicates any subsequent administration.

Amoxicillin should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform (erythematous) rash has been associated with this condition following the use of amoxicillin.

Jarisch-Herxheimer reaction

The Jarisch-Herxheimer reaction has been seen following amoxicillin treatment of Lyme disease (see section 4.8). It results directly from the bactericidal activity of amoxicillin on the causative bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Overgrowth of non-susceptible microorganisms

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Antibiotic-associated colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life threatening (see section 4.8). Therefore, it is important to consider the diagnosis in patients who present with diarrhoea during, or subsequent to, the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin should immediately be discontinued, a physician consulted and appropriate therapy initiated. Anti-peristaltic medicinal products are contra-indicated in this situation.

Prolonged therapy

Periodic assessment of organ system functions; including renal, hepatic and haematopoietic function is advisable during prolonged therapy. Elevated liver enzymes and changes in blood counts have been reported (see section 4.8).

Anticoagulants

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see sections 4.5 and 4.8).

Crystalluria

In patients with reduced urine output, crystalluria (including acute renal injury) has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see sections 4.8 and 4.9).

Interference with diagnostic tests

Elevated serum and urinary levels of amoxicillin are likely to affect certain laboratory tests. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used.

The presence of amoxicillin may distort assay results for oestriol in pregnant women.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin.

Allopurinol

Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Tetracyclines

Tetracyclines and other bacteriostatic drugs may interfere with the bactericidal effects of amoxicillin.

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see section 4.4 and 4.8).

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Oral typhoid vaccine

The oral typhoid vaccine is inactivated by antibacterials.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Limited data on the use of amoxicillin during pregnancy in humans do not indicate an increased risk of congenital malformations. Amoxicillin may be used in pregnancy where the potential benefits outweigh the potential risks associated with treatment.

Breastfeeding

Amoxicillin is excreted into breast milk in small quantities with the possible risk of sensitisation. Consequently, diarrhoea and fungus infection of the mucous membrane are possible in the breast-fed infant, so that breast-feeding might have to be discontinued. Amoxicillin should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

Fertility

There are no data on the effects of amoxicillin on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and skin rash.

The ADRs derived from clinical studies and post-marketing surveillance with amoxicillin, presented by MedDRA System Organ Class are listed below.

The following terminologies have been used to classify the occurrence of undesirable effects.

Very common (≥1/10)

Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100),
Rare (≥1/10,000 to <1/1,000) Very
rare (<1/10,000)
Not known (cannot be estimated from the available data).

Infections and infestations	
Very rare	Mucocutaneous candidiasis
Blood and lymphatic system disorders	
Very rare	Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia. Prolongation of bleeding time and prothrombin time (see sections 4.4).
Immune system disorders	
Very rare:	Severe allergic reactions including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis (see section 4.4)
Not Known	Jarisch-Herxheimer reaction (see section 4.4).
Nervous system disorders	
Very rare	Hyperkinesia, dizziness and convulsions.(see section 4.4)
Not known	Aseptic meningitis
Cardiac disorders	
Not known	Kounis syndrome (see section 4.4).
Gastrointestinal disorders	
Clinical trial data	
*Common	Diarrhoea and nausea
*Uncommon	Vomiting
Post-marketing data	
Very rare	Antibiotic associated colitis including pseudomembranous colitis and haemorrhagic colitis (see section 4.4). Black hairy tongue
Not known	Drug-induced enterocolitis syndrome

Hepatobiliary disorders	
Very rare	Hepatitis and cholestatic jaundice. Moderate rise in AST and/or ALT.
Skin and subcutaneous tissue disorders	
Clinical trial data	
*Common	Skin rash
*Uncommon	Urticaria and pruritus
Post-marketing data	
Very rare	Skin reactions such as erythema multiforme and Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP) (See section 4.4) and drug reaction with eosinophilia and systemic symptoms (DRESS).
Not known	Linear IgA disease
Renal and urinary tract disorders	
Very rare	Interstitial nephritis
Not known	Crystalluria (including acute renal injury see section 4.4 and 4.9 Overdose)
*The incidence of these AEs was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.	

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the yellow card scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App store.

4.9Overdose

Symptoms and signs of overdose

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of the fluid and electrolyte balances may be evident.

Amoxicillin crystalluria, in some cases leading to renal failure, has been observed.

Convulsions may occur in patients with impaired renal function or in those receiving high doses (see section 4.4 and 4.8).

Treatment of intoxication

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance.

Amoxicillin may be removed from the circulation by haemodialysis. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see section 4.4).

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: penicillins with extended spectrum; ATC code: J01CA04.

Mechanism of action

Amoxicillin is a semisynthetic, broad-spectrum, beta-lactam penicillin antibiotic that inhibits one or more enzymes (often referred to as penicillin- binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Pharmacokinetic/pharmacodynamic relationship

The time above the minimum inhibitory concentration (T>MIC) is consider to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The main mechanisms of resistance to amoxicillin are:

- Inactivation by bacterial beta-lactamases
- Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.

Impermeability of bacteria or efflux pump mechanism may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Breakpoints

MIC breakpoints for amoxicillin are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) version 11.0.

Organism	Susceptibility Breakpoints (µg/ml)	
	Susceptible	Resistant
Haemophilus influenzae[1]	≤ 0.001	> 2
Moraxella catarrhalis	Note [2]	Note [2]
Staphylococcus spp.	Note [3, 4, 5]	Note [3, 4, 5]
Enterococcus spp.[6]	≤ 4 [7]	> 8[7]
Streptococcus groups A, B, C, G (indications other than meningitis)	Note [8]	Note [8]
Streptococcus pneumoniae[9]	≤ 0.5	> 1
Enterobacterales [10]	≤ 8	> 8
Gram-negative Anaerobes [11]	≤ 0.5	> 2

Gram-positive Anaerobes [11] (except *Clostridioides difficile*)	≤ 4	> 8
Non-species related breakpoints	≤ 2	> 8
Viridans group streptococci	≤0.5	>2
Pasteurella multocida	≤1	>1
Helicobacter pylori	≤0.125	>0.125
Neisseria meningitidis (indications other than meningitis)	≤0.125	>1

[1] Beta-lactamase positive isolates can be reported resistant to ampicillin, amoxicillin and piperacillin without inhibitors. Tests based on a chromogenic cephalosporin can be used to detect the beta-lactamase.

[2] Most *M. catarrhalis* produce beta-lactamase, although beta-lactamase production is slow and may give weak results with *in vitro* tests. Beta-lactamase producers should be reported resistant to penicillins and aminopenicillins without inhibitors.

[3] Most *S. aureus* are penicillinase producers and some are methicillin resistant. Either mechanism renders them resistant to benzylpenicillin, phenoxymethylpenicillin, ampicillin, amoxicillin, piperacillin and ticarcillin. Isolates that test susceptible to benzylpenicillin and cefoxitin can be reported susceptible to all penicillins. Isolates that test resistant to benzylpenicillin but susceptible to cefoxitin are susceptible to β-lactam β-lactamase inhibitor combinations, the isoxazolylpenicillins (oxacillin, cloxacillin, dicloxacillin and flucloxacillin) and nafcillin. For agents given orally, care to achieve sufficient exposure at the site of the infection should be exercised. Isolates that test resistant to cefoxitin are resistant to all penicillins.

[4] Most coagulase-negative staphylococci are penicillinase producers and some are methicillin resistant. Either mechanism renders them resistant to benzylpenicillin, phenoxymethylpenicillin, ampicillin, amoxicillin, piperacillin and ticarcillin. No currently available method can reliably detect penicillinase production in coagulase-negative staphylococci but methicillin resistance can be detected with cefoxitin as described.

[5] Ampicillin susceptible *S. saprophyticus* are mecA-negative and susceptible to ampicillin, amoxicillin and piperacillin (without or with a beta-lactamase inhibitor).

[6] Aminopenicillin breakpoints in enterococci are based on intravenous administration. For oral administration the breakpoints are relevant for urinary tract infections only.

[7] Susceptibility to ampicillin, amoxicillin and piperacillin (with and without beta-lactamase inhibitor) can be inferred from ampicillin. Ampicillin resistance is uncommon in *E. faecalis* (confirm with MIC) but common in *E. faecium*.

[8] The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility (indications other than meningitis) with the exception of phenoxymethylpenicillin and isoxazolylpenicillins for streptococcus group B.

[9] The oxacillin 1 μg disk screen test or a benzylpenicillin MIC test shall be used to exclude beta-lactam resistance mechanisms. When the screen is negative (oxacillin inhibition zone ≥20 mm, or benzylpenicillin MIC ≤0.06 mg/l) all beta-lactam agents for which clinical breakpoints are available, can be reported susceptible without further testing, except for cefaclor, which if reported, should be reported as “susceptible, increased exposure” (I). When the screen is positive (inhibition zone <20 mm, or benzylpenicillin MIC >0.06 mg/l), refer to EUCAST flow chart.

[10] Aminopenicillin breakpoints in Enterobacterales are based on intravenous administration. For oral administration the breakpoints are relevant for urinary tract infections only. Breakpoints for other infections are under review.

[11] Susceptibility to ampicillin, amoxicillin, piperacillin and ticarcillin can be inferred

from susceptibility to benzylpenicillin.

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

***In vitro* susceptibility of micro-organisms to Amoxicillin**
Commonly Susceptible Species
Gram-positive aerobes: *Enterococcus faecalis* Beta-hemolytic streptococci (Groups A, B, C and G) *Listeria monocytogenes*
Species for which acquired resistance may be a problem
Gram-negative aerobes: *Escherichia coli* *Haemophilus influenzae* *Helicobacter pylori* *Proteus mirabilis* *Salmonella* typhi *Salmonella* paratyphi *Pasteurella multocida*
Gram-positive aerobes: Coagulase negative staphylococcus *Staphylococcus aureus*£ *Streptococcus pneumoniae* Viridans group streptococcus
Gram-positive anaerobes: *Clostridium* spp.
Gram-negative anaerobes: *Fusobacterium* spp.
Other: *Borrelia burgdorferi*
Inherently resistant organisms†
Gram-positive aerobes: *Enterococcus faecium*†
Gram-negative aerobes: *Acinetobacter* spp. *Enterobacter* spp.

Klebsiella spp. *Pseudomonas* spp.
Gram-negative anaerobes: *Bacteroides* spp. (many strains of *Bacteroides fragilis* are resistant).
Others: *Chlamydia* spp. *Mycoplasma* spp. *Legionella* spp.
† Natural intermediate susceptibility in the absence of acquired mechanism of resistance. £ Almost all *S.aureus* are resistant to amoxicillin due to production of penicillinase. In addition, all methicillin-resistant strains are resistant to amoxicillin.

5.2 Pharmacokinetic properties

Absorption

Amoxicillin fully dissociates in aqueous solution at physiological pH. It is rapidly and well absorbed by the oral route of administration. Following oral administration, amoxicillin is approximately 70% bioavailable. The time to peak plasma concentration (T_{max}) is approximately one hour.

The pharmacokinetic results for a study, in which an amoxicillin dose of 250mg three times daily was administered in the fasting state to groups of healthy volunteers, are presented below.

C_{max}	T_{max}*	AUC (0-24h)	T ½
(µg/ml)	(h)	(µg.h/ml)	(h)
3.3 ± 1.12	1.5 (1.0-2.0)	26.7 ± 4.56	1.36 ± 0.56
*Median (range)			

In the range of 250 to 3000mg the bioavailability is linear in proportion to dose (measured as C_{max} and AUC). The absorption is not influenced by simultaneous food intake.

Haemodialysis can be used for elimination of amoxicillin.

Distribution

About 18% of total plasma amoxicillin is bound to protein and the apparent volume of distribution is around 0.3 to 0.4 l/kg.

Following intravenous administration, amoxicillin has been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.

From animal studies there is no evidence for significant tissue retention of drug-derived material. Amoxicillin, like most penicillins, can be detected in breast milk (see section 4.6).

Amoxicillin has been shown to cross the placental barrier (see section 4.6).

Biotransformation
Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25% of the initial dose.

Elimination
The major route of elimination for amoxicillin is via the kidney.

Amoxicillin has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/hour in healthy subjects. Approximately 60 to 70% of the amoxicillin is excreted unchanged in urine during the first 6 hours after administration of a single 250mg or 500mg dose of amoxicillin. Various studies have found the urinary excretion to be 50-85% for amoxicillin over a 24 hour period

Concomitant use of probenecid delays amoxicillin excretion (see section 4.5).

Age
The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Gender
Following oral administration of amoxicillin to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of amoxicillin.

Renal impairment
The total serum clearance of amoxicillin decreases proportionately with decreasing renal function (see sections 4.2 and 4.4).

Hepatic impairment
Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development.
Carcinogenicity studies have not been conducted with amoxicillin.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium Stearate Ph. Eur
Maize Starch Ph. Eur

Capsule Shell
Erythrosin E127
Quinoline Yellow E104
Titanium Dioxide E171
Red Iron Oxide E172
Gelatin NF

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Do not store above 25^{o}C. Protect from light and moisture.

6.5 Nature and contents of container

An opaque white polypropylene securitainer with a polyethylene air proof security cap.
15, 18, 20, 21, 28, 30, 50, 100 or 500 capsule pack sizes contain a polyethylene jayfilla
1000 capsule pack size contain a polyethylene bag.

Or an opaque PVDC/PVC blister 250/40 with an aluminium lidding foil 20 micron containing 15, 18, 20, 21, 28, 30, 50, 100, 500 or 1000 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Kent Pharmaceuticals Limited, Connect 38, 1, Dover Place, Ashford, Kent, United Kingdom. TN23 1FB

8 MARKETING AUTHORISATION NUMBER(S)

PL 08215/0175

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/02/2012

10 DATE OF REVISION OF THE TEXT

21/10/2025